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RESEARCH ARTICLE

MICROBIAL COMMUNITIES IN HEALTHY ORAL MUCOSA.

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Abstract

Understanding what constitutes microbial communities in health, as opposed to disease, is a crucial goal in studying the microbiology of the human mouth, the portal of entry to both the gastrointestinal(GI) and respiratory tracts. The mouth houses the second most diverse microbial community in the body, harboring over 700 species of bacteria that colonize the hard surfaces of teeth and the soft tissues of the oral mucosa. Through recent advances in technology, we have started to unravel the complexities of the oral microbes and gained new insights into its role during both health and disease. Perturbations of the oral microbes through modern-day lifestyles can have detrimental consequences for our general and oral health.

Introduction:-

Acc to WHO 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. Oral microbiology is the study of the microorganisms of the oral cavity and the interactions between the oral microorganisms with each other and with the host & refers to the population of microorganisms that inhabit skin and mucous membranes of normal healthy skin. The mouth is inhabited by an indigenous "normal" microflora that is composed of over 500 species—the majority still uncultivable. Certain microbial types are constantly found in the specific oral areas. These microbial types are referred to collectively as the normal, indigenous, or resident floras and constitute the oral ecosystems.[2] The normal flora can be divided into two groups:

Normal or resident flora:
Some organisms are almost always present in a normal oral cavity and constitutes constant/normal microbial flora. It is further divided into two types: indigenous & supplemental.

Indigenous**:** comprise of those species that almost always present in high numbers (> 1%) in a particular site, such as the supra gingival plaque, the surface of the tongue. There numerical dominance implies that they are compatible with the host and entered into a stable relationship with the host.[3]

Supplemental**:** The supplemental flora comprises the species that are nearly present but are in low numbers (<1%). These organisms may become indigenous if the environment changes. **Transient:** Certain microbes tend to stay for a short time in the oral cavity of a few individuals. If the resident flora is intact, there is very little significance of the transient flora. However if the normal flora is disturbed, the transient flora may proliferate and produce disease.[4]
In addition to the normal & transient microfloras, a third or intermediate group, the **supplemental** (normal) flora has been designated. It represents those microorganisms that may be detected in a significant percentage of

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individuals. Persons harboring supplemental normal flora generally possessing them in moderate numbers & for long periods of time.[4]

Beneficial role of resident flora:

1. They prevent or suppress the colonization/ invasion of the body by pathogens by bacterial interference.
2. Members of the resident flora in the intestinal tract synthesize vitamins, especially vitamin K and several B vitamins.
3. Antibodies produced in response to commensals cross react with pathogens thus raising the immune status of the host.
4. Bacteriocins produced by some microorganisms of normal flora have harmful effect on pathogens.
5. The endotoxins liberated by them may help the defence mechanism of the body by triggering the alternative complement pathway.

The relationship between humans & their oral microflora begins shortly after birth & lasts a lifetime. Soon after birth, we begin to acquire a complex consortium of micro-organisms by salivary transmission associated with intimate human contact (Carlsson et al., 1975).

The mouth contains both distinct mucosal (lips, cheek, tongue, palate) and, uniquely, non-shedding surfaces (teeth) for microbial colonization. Each surface harbours a diverse but characteristic microflora, the composition and metabolism of which is dictated by the biological properties of each site. The resident oral microflora develops in an orderly manner via waves of microbial succession (both autogenic and allogenic). Pioneer species (many of which are s IgA protease-producing streptococci) colonize saliva-coated surfaces through specific stereo-chemical, adhesion-receptor interactions. The metabolism of these organisms modifies local environmental conditions, facilitating subsequent attachment and growth by later, and more fastidious, colonizers. Eventually, a stable biofilm community develops, that plays an active role in (a) the normal development of the physiology of the habitat, and (b) the innate host defences (colonization resistance). [5]

Cheek mucosa encourages the establishment of predominantly facultative types, especially viridians streptococci. The gingival crevice (where exudates fluid flows) creates an environment favourable for anaerobic and facultative microbial communities, whereas the tooth surface has an environment that encourages the residence of aerobic, facultative, and anaerobic microfloras.[2]

In healthy mouth, ‘‘good’’ bacteria and other microbes compete with nefarious cousins and keep them in check. But if conditions change, pathogenic microbes can gang up against the beneficial species and gain control of the mouth’s surfaces. Bleeding gums, cavities, and bad breath can result.[6]

Oral bacteria include Streptococci, Lactobacilli, Staphylococci, Corynebacteria, and various anaerobes in particular bacteroides. Some fungal forms are also found in the oral cavity as normal commensal out of which Candida albicans is the most commonest fungus isolated from the oral cavity. Some protozoans are also seen in periodontal lesions. Viruses may be present during active infections or asymptomatic carrier stages.

Certain areas in the oral environment show differences in oxygen tension and in nutrition. Some surfaces protect the organism from friction and the flow of oral secretions, whereas other surfaces do not. The oral cavity represents a host environment, possessing features that favour the established location and growth of a variety of microorganisms. Those microorganisms that grow best in the absence of oxygen or at a low oxygen tension in a mixed community live in those niches in which oxygen is reduced or eliminated. For example, the spirochete Treponema microdentium is dependent on other organisms and the anaerobic environment of the gingival crevice for the survival.[7]

The intrinsic sources of nutrients for microorganisms in the oral cavity are the gingival crevice fluid materials around the teeth, the pus cells and the epithelial cells undergoing degradation, and the salivary components. Whole saliva has been found to contain 18 free amino acids, including aspartic acid, glutamic acid, threonine, serine, glycine, alanine, phenylalanine, leucine, isoleucine, proline, cystine, valine, methionine, tyrosine, tryptophan, histidine, lysine and arginine. Saliva from caries free subjects supports better growth of S. mutans (type c) than saliva from carious subjects. This difference appears to be associated with certain protein in caries free saliva.[8,9]

1. Human acquisition of oral microflora
2. The oral cavity might be considered an ideal microbial incubator. It possesses a temperature of approximately 35^0- 36^0C and has an abundance of moisture, an excellent supply of various types of foods, and differences in oxygen tension. Many aerobic, facultative, and anaerobic types find conditions favourable for their growth.
3. In the oral cavity the microfloras differ basically in the oral anatomy. The microbial population that forms on the surfaces of the crowns of teeth differ collectively from those microbial forms that inhabit the gingival pocket, and these differ from those found on the tongue and mucous membrane of the cheek. The salivary microbial population represents those microbial forms that are freed from all oral surfaces as the result of the washing effect of the saliva.[4]
4. Studies of the indigenous human oral flora should begin with the first appearance of micro-organisms in the oral cavity. This means that analysis of oral flora should begin with the newborn. Until the time of birth the human infant is usually "germfree." The newborn then becomes suddenly exposed to millions of microorganisms, only a small portion of will become part of his normal microflora.[10]

The mouth of the baby may be sterile or may be contaminated with several types of microorganisms, including streptococci, staphylococci, coliform bacilli, and gram positive rods. The source of these bacteria is the environment to which the child is gradually exposed during and after birth. The child comes in contact with the microflora of the mother's vagina and then with the local environment of the outside world. The early oral microflora after birth is mainly aerobic and facultatively anaerobic.

S. salivarius establishes itself early in the oral cavity of infants. In one study S. salivarius was isolated from most infants the day after birth and represented less than 1% of the total number of cultivated bacteria.**[10]** (it is noted that in the newborn the mucosa is unable to bind streptococci ; this may explain the low level of bacteria colonization during the first 48 hours of life).

In a later study this organism was detected in the oral cavity within 18 hours after birth and was shown to be the same serotype as that of the mother. This is not surprising, since this organism normally resides on the tongue and oral mucous membranes that are washed by saliva and becomes part of the salivary flora.**[11]** S. salivarius thus may be directly transferred by the mother to the infant**.** S. sanguis has been demonstrated in the mouth of infants only after the eruption of teeth, whereas S. mutans is not isolated during the first year**.[12,13]** S. mutans is reported to have been isolated from primary dentition by the time the molars erupt. Recently it was shown that S. mutans could establish itself in predentate infants with acrylate cleft palate obturators and in those infants having only primary incisors. Serotype c is the most common of the S. mutans isolated.**[14,15]**

The anaerobe Veillonella alcalescens occasionally has been isolated from infants less than 2 days old and regularly from infants after 1 week. The anaerobic fusiform bacilli have been cultivated from the mouths of infants younger than 2 months and from nearly all infants before the eruption of the first incisors. Fusiform bacilli appear to increase in number during the 4^{th} and 8^{th} months, and Peptostreptococcus anaerobius is reported to make its appearance in infants older than five months. The dominant flora of the oral cavity of the child before the eruption of the teeth is mainly facultative in nature; with the eruption of the teeth there is an increase in anaerobic forms. Lay and Russell reported that the prevalence of candida species in the mouths of 140 infants were taken home, the prevalence rose to 82% at the age of 1 month and then declined to 60% by 8 months of age. There was no correlation between the presence of maternal vaginal candida and candida in the mouths of infants.**[16]** The quantitative and qualitative relationships of oral microorganisms change with the appearance of the dentition, the loss of the dentition, the use of artificial dentures, the type of the diet, the subject's oral hygienic practices, and the degree of health & disease.
With the eruption of teeth there is an increase in anaerobic forms, such as Leptotrichia, spirochaetes, fusiform bacilli, spiral forms, and vibrio. With partial loss of teeth, this microflora persists only where the teeth remain. The presence of fusiform bacilli and spirochetes appears to be associated with the natural dentition. Complete loss of dentition causes a reversion of microflora to a predominantly aerobic facultative type. Anaerobic forms generally reappear with the wearing of the dentures. S. sanguis and S. mutans have been shown to disappear in the edentulous mouth and reappear with the wearing of the denture.**[17]**

The surface pioneers
Oral microbial communities mainly exist as biofilms on saliva-bathed surfaces and, in this respect, provide model structures for studies of biofilm formation in a wide range of ecosystems. The underlying principle in the initiation of community development is the adhesion of primary microorganisms to a surface. The pioneer organisms then

provide a new surface and appropriate metabolic and other signals for the attachment of succeeding organisms. The pioneer bacteria that first engage receptors for adhesion in the oral cavity include many species of Streptococcus. More than 60% of the bacteria found in early communities on saliva-coated tooth enamel are streptococci.[18] Other bacterial genera that are amongst the early colonizers include Actinomyces ,Veillonella and Neisseria. Initial adhesion invariably involves binding of bacteria to saliva components that are adsorbed to the oral cavity surfaces. The specific components adsorbed depend upon the composition of the surface, thus different surfaces present different salivary receptors. Moreover, some salivary receptors, termed cryptitopes, only attain an active configuration after binding to a surface. The proline-rich proteins and statherin components of saliva are tightly bound by enamel, presenting peptide epitopes and cryptitopes for recognition by streptococci.

Salivary mucins and agglutinins, such as gp340 glycoprotein[19] also adsorb to enamel and to epithelial surfaces and provide receptors for streptococci and other early colonizing bacteria. In fact, an array of proteins in saliva, including a-amylase, immunoglobulins, fibronectin, lactoferrin and alpha 2-macroglobulin, have been shown to be bound by streptococci and thus potentially all provide receptors for adhesion. The ability of the early colonizing bacteria to express multiple adhesins probably confers a major selective advantage over those bacteria that have less versatility in receptor recognition. Mechanisms of initial bacterial adhesion include recognition of oligosaccharide receptors by protein adhesins, in lectin-like reactions protein–protein interactions[20] and ionic or hydrophobic associations between microbial surface components and the adhesion substratum.

Some of the important streptococcal adhesions include the antigen I/II family polypeptides, which bind gp340, fibronectin and collagen. These enable streptococcal attachment to salivary pellicle, host cells and exposed root dentine.

The primary colonizers have a remarkable capacity to adhere tenaciously to surfaces, even under high shear stress forces and in the presence of an excess of soluble receptors in fluid phase. These properties might be conferred by adhesions that respond positively to fluid flow stresses and that can discriminate between immobilized or fluid phase isoforms of the same receptor.

Building early communities

The structure of a community is dependent upon the nature of the foundations. This is illustrated by the finding that colonization of newly erupted teeth by Streptococcus sanguis at an early age is correlated with delayed colonization of cariogenic Streptococcus mutans and, therefore, lower rates of tooth decay.[21]

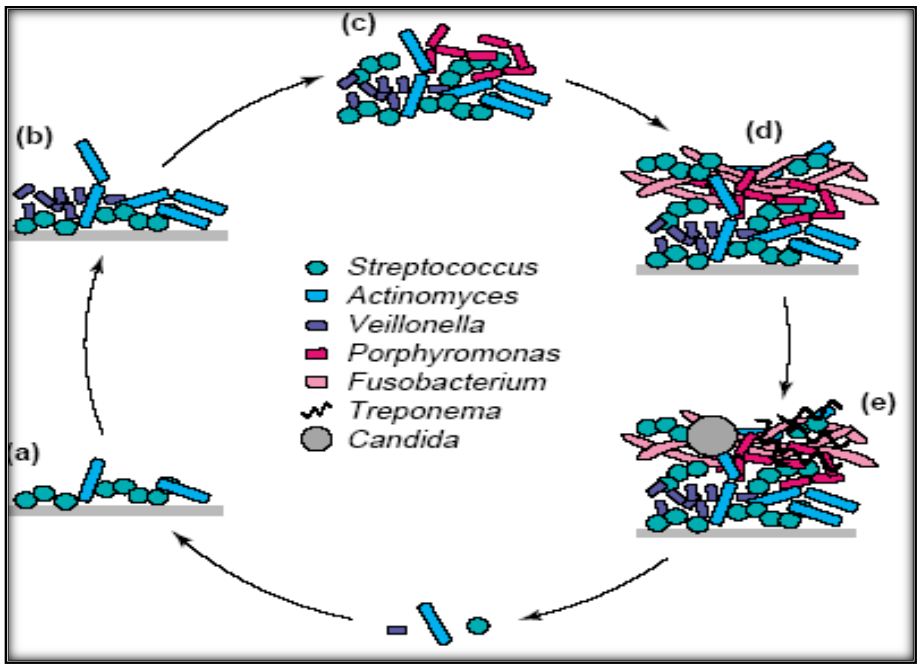
The concept of getting the right bacterium to colonize at the right time is pertinent to the idea that colonization by one organism could retard or prevent colonization by another. Thus, provision of a healthy colonizer to the mouth, nose or gut, might be beneficial towards establishing microbial communities that are agonistic rather than antagonistic. In the initial development of oral microbial communities, specific associations between the pioneering species and subsequently colonizing bacteria have been identified that are believed to contribute to community development. Therefore, interactions between streptococci and Actinomyces, involving lectin-carbohydrate and protein–protein interactions are commonly reported.[22]

Metabolic associations between streptococci and Veillonella[23] appear to be mutually beneficial. Interactions between species can be highly specific, for example, to the extent that the antigen I/II family protein adhesin SspB on S. gordonii recognizes only subgroups of Actinomyces naeslundii. The physical associations between species or societies of oral bacteria found at various oral cavity sites. Probably it reflect close metabolic synergies or dependencies for effective growth and survival. A simple example relates to the differing abilities of oral streptococci to metabolize host glycoproteins. A cohort of streptococcal species expressing different arrays of glycan hydrolyases[24] is more efficient in overall glycoprotein breakdown than are the individual species, thus, all members of the cohort benefit.

Constructing complex consortia

The components of microbial communities found at different oral cavity sites are quite variable. Part of the reason for this is that the microbial building blocks of these communities might be distinct. Bacteria that first adhere to a site do so because of the biological properties and numbers of the receptors that are available. Complex consortia then develop through recognition of the other community members, metabolic signals or attractants, availability of usable substrates, adherent substrates and deposited host salivary molecules. Potential pathogens, such as

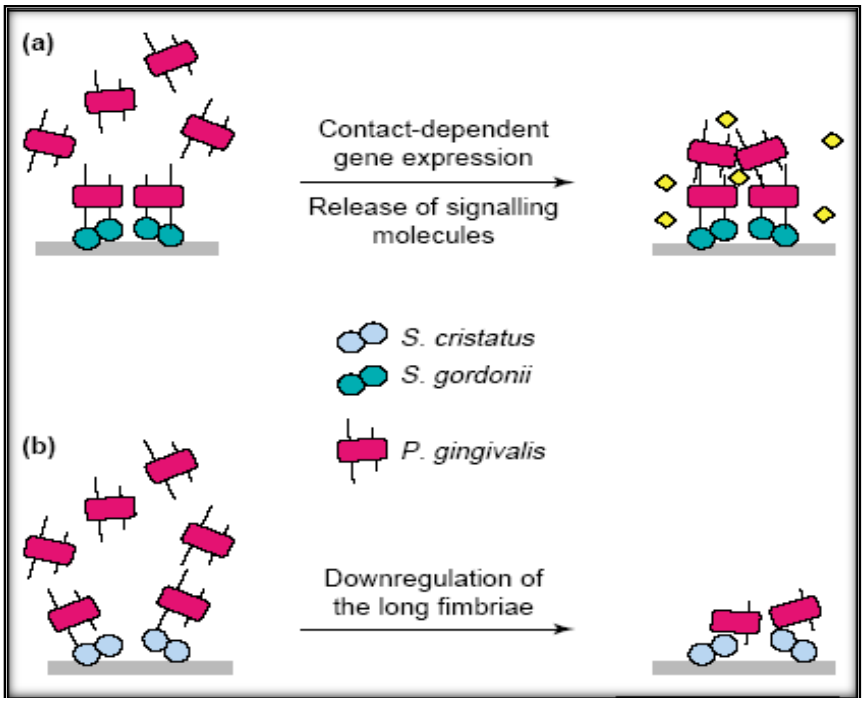
Fusobacterium nucleatum and P. gingivalis, are characteristically found as components of complex communities and are rarely seen in appreciable numbers in the early building communities of streptococci, Actinomyces and Veillonella.[25]



A day in the life of an oral microbial community

1. The freshly cleaned tooth surface is quickly coated with a salivary pellicle and then by primary colonizing bacteria, such as species of Streptococcus and Actinomyces.
2. These provide a linking film for the subsequent attachment and accumulation of other bacteria, such as Veillonella and Actinomyces, that form close metabolic relationships with streptococci.
3. As local environments develop within the community, the retention of bacteria like Porphyromonas in association with streptococci is favoured.
4. Anaerobic conditions also encourage the incorporation of Fusobacterium, which interacts with a remarkably wide spectrum of plaque bacteria and has, therefore, been suggested to be an important bridging component in oral microbial communities.
5. The incorporation of Fusobacterium and Porphyromonas probably also facilitates the growth of Treponema, part of the so-called red group of periodontal pathogens, and with host immunity compromized, the inclusion of yeasts (e.g. Candida albicans) into the sub-gingival plaque community. Plaque contains hundreds of different species of microorganisms in a matrix of host salivary molecules and bacterial extracellular products.[25]

It is probable that many organisms would not be able to exist within the human oral microbial ecosystem if they were not embraced within a mixed community. This is why understanding what comprises a healthy microbial community and devising ways of promoting such communities could encourage health instead of sickness. Laboratory studies support the concept that colonization by P. gingivalis might be dependent upon other bacteria. Colonization of saliva-coated surfaces and penetration of dentin is facilitated by the presence of antecedent streptococci. Multivalent co-adhesive interactions characterize the binding of P. gingivalis to oral streptococci such as Streptococcus gordonii.



Schematic representation of outcomes that follow P. gingivalis binding to S. gordonii or to S. cristatus

1. P. gingivalis (red) attaches to S. gordonii (green) through adhesion mechanisms mediated by both the long and short fimbriae. P. gingivalis short fimbriae binding to the S. gordonii AgI/II family protein adhesins induces changes in gene expression in P. gingivalis. Combined with the presence of potential extracellular signalling molecules (yellow), this stimulates recruitment of additional P. gingivalis cells from the fluid phase and subsequent accretion of a mixed biofilm microcolony.
2. P. gingivalis (red) attachment to S. cristatus (blue) is mediated by the long fimbriae. Contact with S. cristatus induces downregulation of fimA transcription and the long fimbriae are lost. Only lower affinity attachment remains and the signals necessary for biofilm formation do not occur.[25]

Normal microbial flora of oral cavity[4]
In the gingival crevice

Group	Genera and/or species commonly found
Gram positive facultative cocci (28.8 %)	Staphylococci Enterococci Streptococcus mutans Streptococcus sanguis Streptococcus mitis
Gram positive anaerobic cocci (7.4%)	Peptostreptococcus
Gram positive facultative rods (15.3%)	Corynebacterium Lactobacillus Nocardia Odontomyces viscosus Bacterionema matruchotii
Gram positive anaerobic rods (20.2%)	Actinomyces bifidus Actinomyces israelii Actinomyces naeslundii Actinomyces odontolyticus

	Propionibacterium acnes Leptotrichia buccalis Corynebacterium
Gram negative facultative cocci (0.4%)	Neisseria
Gram negative anaerobic cocci (10.7%)	Veillonella alcalescens Veillonella parvula
Gram negative facultative rods (1.2%)	--
Gram negative anaerobic rods (16.1%)	Bacteroides melanogenicus Bacteroides oralis Vibrio sputorum Fusobacterium nucleatum Selenomonas sputigena
Spiral organisms (1 to 3)	Treponema denticola Treponema oralis Treponema macrodentium Borellia vincenti

Tongue microflora

1. Facultative streptococci 38.3%
2. Veilonella 14.5%
3. Facultative diphtheroids 13.0%
4. Anaerobic diphtheroids 7.4%
5. Micrococci-staphylococci 6.5%
6. Bacteroides 5.3%
7. Peptostreptococcus-peptococcus 4.2%
8. Neisseria 2.3%
9. Vibrio 2.1%
10. Fusobacterium 0.8%
11. Unidentifiable gram-negetative rods 3.2%
12. Unidentifiable gram-negetative cocci 2.6%

Salivary microflora

Dislodgment of microorganisms from colonizing aggregations in various locations of oral cavity(the teeth, tongue, cheek, & pharyngeal mucous membrane) contributes to the microflora of the saliva.[26] Adult human saliva is reported to contain approximately 6 billion ($6x10^9$) microorganisms per mililitre including streptococci, peptostreptococci, Veillonella, Corynebacterium, Neisseria, Nocardia, Fusobacterium, Bacteroides, lactobacilli, Actinomyces, spirochaetes. Yeasts, protozoa, and others. Investigations of the possible source of salivary bacteria indicates that 47% of the facultative streptococci present in saliva, 21% to 55 % of the facultative streptococci on the tongue, and 10% of the facultative streptococci on the cheek. Dental plaque is not considered to be the source of S. salivarius found in saliva. Although S.sanguis is reported to be the dominant streptococci in early plaque from teeth.It constitutes only a minor portion of the flora of other sites in the oral cavity.[26] So, dental plaque is not the major contributor to the salivary microflora. Major source appears to be the tongue.

Approximate proportional distribution of bacteria on various oral surfaces[27]

Bacteria	Gingival crevice	Coronal plaque	Tongue dorsum	Buccal mucosa	saliva
Streptococcus salivarius	<0.5	<0.5	20	11	20
Streptococcus mitis	8	15	8	60	20
Streptococcus sanguis	8	15	4	11	8
Streptococcus mutans	?	0-50	<1	<1	<1
Enterococci	0-10	<0.1	<0.01	<0.1	<0.1

Gram positive filaments	35	42	20	?	15
Lactobacilli	<1	<0.005	<0.1	<0.1	<1
Veillonella spp.	10	2	12	1	10
Neisseria spp.	<0.5	<0.5	<0.5	<0.5	<1
Bacteroides oralis	5	5	4	?	?
Bacteroides melanogenicus	6	<1	<1	<1	<1
Vibrio sputorum	5	1	<0.5	<0.5	?
Spirochetes	2	<0.1	<0.1	<0.1	<0.1
Fusobacterium spp.	3	4	1	?	<1

Microbial adherence and aggregation in the oral cavity

The ecologic relationship of microorganisms with the oral cavity is perhaps more dependent on the ability of the organisms to attach to specific oral tissues than on their association with the nutritional factors of the specific tissue or the area. Organisms that cannot attach to specific oral surfaces would be expected to be more easily removed by salivary flow and the flow of oral secretions.[4]

Recently, considerable research has been concerned with the ability of oral micro-organisms to adhere to different oral surfaces. Early work has demonstrated that S. sanguis appears to have a preference for colonizing on tooth surfaces, whereas S. salivarius has a marked affinity for epithelial surfaces and shows little affinity to adhere to teeth. It has been observed that plaque bacteria, S. sanguis, S. mitis, and Actinomyces species, but not S. mutans or S. salivarius aggregate in presence of human saliva. Also, S. sanguis and Actinomyces have been observed to adhere to saliva coated enamel, whereas lactobacilli, S. mutans and S. salivarius appear to be unaffected or demonstrate little ability to adhere to saliva coated enamel.[28]

Bacteria adsorbed to saliva-coated enamel also are agglutinated by cell free saliva. This affinity between host and saliva explains a method of adherence to teeth in the oral cavity.

Extracellular dextran polymers,[29] an outer capsular slime formed by formed by certain microorganisms, has demonstrated a high affinity for adherence to dental enamel. Dextrans, mainly of the alpha 1.3 linkage, are insoluble and appear to be involved in initiating plaque formation and caries by localizing acidogenic-aciduric bacteria on teeth. The synthesis of extracellular polysaccharides before sorption has been shown to reduce desorption and foster a firm attachment to tooth substance.[30] Completely unrelated strains of bacteria can aggregate by cell to cell interaction.

Such interaction also explains adherence mechanisms in developing dental plaque. Salivary polymers on tooth surface mediate the attachment of S. sanguis, whereas the attachment of S. mutans is mediated mainly by its own extracellular glucans to tooth surfaces. On the other hand, S. salivarius does not appear to attach to saliva coated teeth. Recent studies have demonstrated that S. salivarius and S. mitior (mitis) exhibit morphologically different fibrillar fuzzy surface coatings, whereas S. sanguis, S. mutans and lactobacilli have less fibrillar surfaces.[31]
Fibril hair like structures were observed with the electron microscope for A. naeslundii and A. viscosus. These structures appear on the outer surface, and it is suggested that they provide a mechanism or a structure for adherence of these organisms with one another and with the tooth surface.

Teichoic acid have the potencial to adsorb to tooth enamel. These acids have been found in culture broth of strains of S. mutans, S. sanguis, S. mitis, and S.salivarius; in the cell wall and cell surface membrane of these streptococci; and in the strains of L. casei, L. plantarum, and Lactobacillus fermentum. Cell surface teichoic acids can aid these organisms in the adherence to tooth surfaces and in the formation of dental plaque. The adhesiveness of enamel shown by the capsular coat of S. mutans may in part be the effect of teichoic acid in this capsular coat.[32]

The teichoic acids at the bacterial cell surfaces may be involved in the adsorption of the oral organisms S. pyogenes, S. salivarius, and S. mutans to oral epithelial cells and may also explain their feeble affinity for saliva treated hydroxyapatite.[33]

Many plaque bacteria are capable of hydrolyzing the extracellular levan(fructan) in vitro.[34]

It is suspected that this happens also in vivo because the fructan content of dental plaque from humans varies widely and may drop to levels that can not be detected.[35]

It has been observed that cariogenic S. mutans has not been readily implanted into the human mouth and also is not readily passed between members of families. Although it forms an extra cellular dextran in the presence of dietary sucrose and has an affinity to adhere to tooth enamel, it does not colonize uniformly over surfaces of teeth, nor does it appear to be easily transmitted from one tooth surface to another in the same individual. Recent studies have demonstrated that significant proportion of the human dental plaque bacterial flora produce glucan (dextran)-degradating enzymes.[36]

Some of the bacteria in the mouth are responsible for dental diseases such as caries and periodontal diseases which are one of the most common diseases in humans. At least 35% of adults between 30-80 years in the United States have some form of periodontal disease. Specific oral bacterial species are also considered to have a role in systemic diseases such as bacterial endocarditis, aspiration pneumonia, osteomyelitis in children and cardiovascular diseases.[37]

Concluding Remarks:-

The arguments outlined above clearly demonstrate that the resident oral microflora plays an active role in the normal development of the mouth and in the maintenance of health at a site. Clinicians need to be aware of the beneficial properties of the resident microflora, and their treatment strategies should be focussed on the control rather than the elimination of these organisms, especially in dental plaque. In the future, it may be feasible to target treatment more specifically at particular 'pathogens' (e.g. immunotherapy), or more imaginative approaches could be used to prevent disease. For example, it may be possible to remove the environmental pressures that favour the selection of the organisms associated with disease, and 'prebiotics' (agents that encourage the growth of the normal microflora) and 'probiotics' (the deliberate use of organisms to restore colonisation resistance) may become available. Such approaches are currently finding increasing this volume. Bacteria growing on a surface as a biofilm display an altered phenotype, and are also more resistant to antimicrobial agents.[5]

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